



# The risk of suicide in patients with critical illness A population-based study in Taiwan

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#### **Abstract**

The authors investigated retrospectively the association between critical illness and risk of suicide attempts. The data are from Taiwan's National Health Insurance Research Database. Propensity score matching, multivariable models, Kaplan–Meier analysis, and competing risk analysis were used to explore this association. The authors found that patients having an critical illness were associated with increased risk of suicide attempts after adjusting for risk factors (adjusted hazard ratio = 2.98; 95% confidence interval = 1.46–6.08). Among different subtypes of critical illness, patients with sepsis/septic shock exhibited the highest risk of suicide attempts (adjusted hazard ratio = 3.43, 95% confidence interval = 1.52–7.74). An association between critical illness and suicide attempts was shown. Sepsis/septic shock was found to confer the highest risk in these specific population.

Keywords: critical illness, sepsis, septic shock, suicide

### 1. Introduction

The enormous improvement in critical care is obvious in past years<sup>[1-3]</sup>; however, the psychologic outcomes among patient surviving critical illness obtained relatively less attention because most physicans and investigators focus more effort on the physiological mechanism rather than psychological impact. [4,5] In the modern society, psychologic disorder is increasingly recognized as a huge global burden and the balance and homeostasis of body-mid or physio-psychological inter-relationship have been proposed. [6,7] Indeed, survivors of intensive care are known to be at increased risk of anxiety, depression, and post-traumatic stress disorder, which is associated with increased risk of suicide.[8,9] Several reports have shown an increased risk of suicide and self-harm in patients surviving from critical illnesses, acute stroke and acute myocardial infarction. In this regard, to enhance the global care for these groups who surviving critical illness, the author used a well-validated nationwide dataset to explore this issue. [10] The paper describes a positive multivariate association between a diagnosis of critical illness and subsequent diagnosis of suicide using a robust database and the big sample size.

# 2. Methods

# 2.1. Data source

This retrospective population-based cohort study was designed to assess the relationship between critical illness and the risk of suicide. Data sources conducted in this present study were retrieved from claims data of Taiwan's National

We identified patients who have ever received a critical illness diagnosis from January 1, 2000 to December 31, 2012 as the critical illness group. The critical illness was defined as the following disease: septicemia (ICD-9-CM codes 038), septic shock (ICD-9-CM codes 785.52), acute myocardial infarction (ICD-9-CM codes 410), hemorrhagic stroke (ICD-9-CM codes 430-432) and ischemic stroke (ICD-9-CM 433-438). The index date means the initial diagnostic date of critical illness. Subjects

Health Insurance Research Database (NHIRD), which cov-

ers approximately 99% of Taiwan residents.[10] The National

Health Research Institute receives insurance claims data from

the National Health Insurance Administration and subse-

quently compiles them into NHIRD for research purposes

since 1995. The NHIRD has been extensively used for epi-

demiological studies. The data utilized in this current study

was the Longitudinal Health Insurance Database (LHID

2000), a subset of the NHIRD. The LHID 2000 consists of

1 million randomly collected samples from the NHI sys-

tem in 2000, and contains historical ambulatory and inpa-

tient care data. Diseases were classified on the basis of the

International Classification of Diseases, Ninth Revision, and

Clinical Modification (ICD-9-CM).[11,12] The accuracy and

validity of NHIRD diagnosis codes have been documented.

All personal information was encrypted to preserve patient

anonymity. This study has been approved by the Research

Ethics Committee at China Medical University Hospital

(CMUH104-REC2-115(CR-7)).

2.2. Study population

This study was supported in part by the Taiwan Ministry of Health and Welfare Clinical Trial Center (MOHW109-TDU-B-212-114004), China Medical University (CMU110-AWARD-01), and China Medical University Hospital (DMR-HHC-110-4).

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request

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How to cite this article: Hu W-S, Lin C-L. The risk of suicide in patients with critical illness: a population-based study in Taiwan. Medicine 2022;101:39(e30656).

Received: 21 January 2022 / Received in final form: 18 August 2022 / Accepted: 19 August 2022

http://dx.doi.org/10.1097/MD.000000000030656

without any critical illness during the study period were randomly selected from the same database as the comparison group. Patients under 20 years old or who had a preexisting diagnosis of suicide attempt before the index date were excluded from the study. Patients in the critical illness and non-critical illness cohorts were matched at a ratio of 1:1 on the basis of a propensity score. The propensity score was calculated using the probability of the treatment assignment by using a logistic regression model and included the following baseline variables: year of index, age, and sex.

## 2.3. Outcome and comorbidities

The outcome of interest in this study was suicide (ICD-9-CM codes E950-E959), including liquid or solid poisoning (ICD-9-CM code E950), charcoal burning and poisoning by gases (ICD-9-CM code E952), hanging (ICD-9-CM code E953), cutting/piercing (ICD-9-CM code E956), jumping from high places (ICD-9-CM code E957), and others (ICD-9-CM codes E951, E954, E955, E958, and E959). All patients were followed from the index date to the occurrence of suicide, death, withdrawal from NHI program, or December 31, 2013, whichever came first. The chronic diseases under consideration included schizophrenic spectrum disorders, depressive disorder, alcohol-related illness, anxiety, mental disorders, insomnia, congestive heart failure, hypertension, diabetes mellitus, vascular diseases, Nonend-stage renal disease, end-stage renal disease, chronic obstructive pulmonary disease, malignancy, autoimmune diseases, and liver cirrhosis. The diagnostic accuracy of comorbidities based on ICD-9 codes has been examined in previous studies. Demographic data of monthly income, urbanization level, and occupation category were also collected.

# 2.4. Statistical analyses

The baseline demographic/clinical characteristics of the critical illness and the comparison cohorts were compared. A chi-square test and Student's t-test were used to evaluate the distribution of category and continuous variables for an unmatched cohort. A standardized mean difference (SMD) of ≤0.10 indicates a negligible difference between the 2 matched cohorts. The incidence rates of suicide were calculated as per 10,000 person-years in both cohorts. The crude hazard ratios and 95% confidence intervals (CIs) of suicide occurrence were estimated using Cox proportional hazard regression. Multivariable models were further adjusted for depression, alcohol-related illness, anxiety, insomnia, and liver cirrhosis. We also examined the association between critical illness and suicide stratified by different subtypes of critical illness. The cumulative incidence of suicide during 12 years of follow-up was estimated for subjects with and without critical illness using Kaplan-Meier analysis, and assessed these differences using a log-rank test. We also considered death as a competing factor to estimate subhazard ratios and 95% CIs using the competing-risks regression models.<sup>[13]</sup> The SAS 9.4 statistical package (SAS Institute Inc, NC, USA) was used for the statistical analyses. A 2-sided P value <0.05 indicated statistical significance.

## 3. Results

The demographics for the unmatched and matched cohorts were shown in Table 1. After matching, 48,651 patients in the critical illness cohort and 48,651 patients in the comparison cohort were enrolled in the study with similar distributions of age and gender by the propensity score. The majority of patients were aged 65 years or above, and males accounted for more than half of the patients in each cohort. The mean age was  $65.7 \pm 15.1$  years in the critical illness cohort and  $65.6 \pm 14.9$  in the comparison cohort. Compared with the comparison cohort, patients

with critical illness had a significantly higher proportion of all the considered comorbidities (P < .001). The distribution of monthly income, urbanization level, and occupation category differed between the 2 cohorts (P < .001).

Table 2 discloses the incidence and risk of suicide between the critical illness and comparison cohorts with propensity score. At the end of the study period, the overall incidence rates of suicide in critical illness cohort and comparison cohort were 1.58 and 0.41 per 10,000 person-years, respectively. After adjusting for confounding factors, critical illness cohort had a significantly increased risk of suicide than the comparison cohort (adjusted hazard ratio [aHR] = 2.98; 95% CI = 1.46–6.08). Table 2 also shows that patients with alcohol-related illness tended to have a higher risk for suicide (aHR = 3.86; 95% CI = 1.68–8.84).

Table 3 presents the stratified analyses with propensity score. The age-specific risk of suicide for critical illness cohort relative to comparison cohort was higher in patients aged under 65 years (aHR = 5.52, 95% CI = 1.56–19.50). When stratified by gender, the risk of suicide for critical illness cohort relative to comparison cohort was higher in both groups (aHR = 2.71, 95% CI = 1.03–7.14 in women and aHR = 3.17, 95% CI = 1.11–9.08 in men). Critical illness was significantly associated with an increased risk of suicide in the following sub-groups: patients with 15,000 to 19,999 monthly income, patients with lower urbanization levels, and laborer patients.

Table 4 shows the risk of suicide in patients with different subtypes of critical illness compared to those without critical illness without or with propensity score matching. In comparison to patients without critical illness, patients with septicemia, septic shock (aHR = 3.43, 95% CI = 1.52–7.74) and ischemic stroke (aHR = 3.04, 95% CI = 1.34–6.90) exhibited a significantly higher risk of suicide. Similar results were shown in the unmatched cohort.

Kaplan–Meier survival analysis revealed that the cumulative incidence of suicide occurrence was significantly higher in the critical illness cohort than in the comparison cohort (log-rank test, P < .001) (Fig. 1).

Table 5 shows the subhazard rate of suicide for critical illness patients, with consideration of the competing risk of death. We found that the critical illness cohort still at a significantly higher risk of suicide than did the comparison cohort (aSHR = 2.98, 95% CI = 1.48–6.02).

## 4. Discussion

Using a large-scale database with propensity score matching, multivariable adjustment as well as competing risk method, the study demonstrates an association between critical illness and suicide. Moreover, sepsis/septic shock carried the highest risk among these critical illnesses.

It was possible to identify the mortality rate for suicide of about 13 per 100,000 in Taiwan. [14] A very recent publication based on a Canadian data set had similar findings; this could be consistent with the control group having an abnormally low rate of suicide. [15] Indeed, the large number of patients included is a major advantage of this study. Although some might criticize that the association might simply reflect the impact of comorbid illness since people with critical illness have more prevalence of medical comorbidity. The observation that sepsis/septic shock tended to be the highest risk of suicide attempt was surely a novel finding and deserved to be further highlighted.

The expected hypothesized association implies that further attention to patient surviving critical illness is mandatory. Additionally, the association appears to be higher with a diagnosis of sepsis/septic shock. Except for the impact of multiple comorbidities on the association, other possible biological links cannot be clearly identified primarily due to the methodology drawback of the investigation. Moreover, it is difficult to see a plausible biological mechanism for this,

Comparisons of demographic characteristics and comorbidities in patients with and without critical illness stratified by propensity score matching.

	Critical i	llness unmatched	<i>P</i> -value	Critical illness ma	tched gender, age, and index year	
	No	Yes	,	No	Yes	-
	(N = 622,882)	(N = 50,122)		(N = 48,651)	(N = 48,651)	SMD <sup>2</sup>
Gender			< 0.001			
Women	314,339 (50.5)	21,175 (42.3)		20,046 (41.2)	20,774 (42.7)	0.03
Men	308,543 (49.5)	28,947 (57.8)		28,605 (50.8)	27,877 (57.3)	0.03
Age stratified			< 0.001			
≤49	448,106 (71.9)	7917 (15.8)		7806 (16.0)	7917 (16.3)	0.006
50-64	118,584 (19.0)	12,619 (25.2)		12,544 (25.8)	12,619 (25.9)	0.004
65+	56,192 (9.02)	29,586 (59.0)		28,301 (58.2)	28,115 (57.8)	0.008
Age, mean ± SD†	$42.3 \pm 15.0$	$66.4 \pm 15.4$	< 0.001	$65.6 \pm 14.9$	65.7 ± 15.1	0.008
Monthly income‡			< 0.001			
< 15,000	147,707 (23.7)	16,696 (33.3)	101001	15,243 (31.3)	15,823 (32.5)	0.026
15,000–19,999	284,729 (45.7)	24,632 (49.1)		21,784 (44.8)	24,061 (49.5)	0.094
≥20,000	190,446 (30.6)	8794 (17.6)		11,624 (23.9)	8767 (18.0)	0.145
Urbanization level§	100,440 (00.0)	0704 (17.0)	< 0.001	11,024 (20.0)	0707 (10.0)	0.140
1 (highest)	194,224 (31.2)	12,310 (24.6)	<b>\0.001</b>	13,758 (28.3)	11,947 (24.6)	0.09
2	184,525 (29.6)	13,296 (26.5)		13,065 (26.9)	12,917 (26.6)	0.03
3	114,801 (18.4)	8721 (17.4)		8189 (16.8)	8489 (17.5)	0.007
4 (lowest)	129,332 (20.8)	15,795 (31.5)		13,639 (28.0)	15,298 (31.4)	0.02
Occupation category	129,332 (20.0)	13,793 (31.3)	-0.001	13,039 (20.0)	13,290 (31.4)	0.00
1 0 111	057.040.(57.4)	17 000 (05 0)	< 0.001	10.070 (40.0)	17 000 (05 0)	0.11
Office worker	357,642 (57.4)	17,660 (35.2)		19,879 (40.9)	17,293 (35.6)	0.11
Laborer	186,111 (29.9)	22,185 (44.3)		19,430 (33.9)	21,574 (44.3)	0.09
Other	79,129 (12.7)	10,277 (20.5)		9342 (19.2)	9784 (20.1)	0.02
Comorbidity	40.40.70.00)	500 (4.00)	0.004	000 (0.40)	F07 (1 00)	0.00
Schizophrenia	4249 (0.68)	532 (1.06)	< 0.001	209 (0.43)	527 (1.08)	0.08
Depression	18,806 (3.02)	3493 (6.97)	< 0.001	2194 (4.51)	3408 (7.00)	0.11
Alcohol-related illness	15,325 (2.46)	3766 (7.51)	< 0.001	1392 (2.86)	3740 (7.69)	0.22
Anxiety	65,092 (10.5)	11,060 (22.1)	< 0.001	8796 (18.1)	10,738 (22.1)	0.10
Mental disorders	40,736 (6.54)	8546 (17.1)	< 0.001	5660 (11.6)	8147 (16.8)	0.15
Insomnia	175,563 (28.2)	29,835 (59.5)	< 0.001	21,967 (45.2)	28,809 (59.2)	0.28
Congestive heart failure	5093 (0.82)	6257 (12.5)	< 0.001	2121 (4.36)	5914 (12.2)	0.29
Hypertension	92,870 (14.9)	34,719 (69.3)	< 0.001	22,350 (45.9)	33,593 (69.1)	0.48
Diabetes mellitus	24,688 (3.96)	13,273 (26.5)	< 0.001	5502 (11.3)	13,031 (26.8)	0.40
Vascular diseases	41,121 (6.60)	20,249 (40.4)	< 0.001	11,556 (23.8)	19,493 (40.1)	0.36
Non-ESRD CKD	4292 (0.69)	4195 (8.37)	< 0.001	1315 (2.70)	4043 (8.31)	0.25
ESRD	890 (0.14)	1250 (2.49)	< 0.001	156 (0.32)	1233 (2.53)	0.19
COPD	30,602 (4.91)	12,563 (25.1)	< 0.001	8530 (17.5)	11,835 (24.3)	0.17
Malignancy	8150 (1.31)	5184 (10.3)	< 0.001	1951 (4.01)	5040 (10.4)	0.25
Autoimmune diseases	645 (0.10)	107 (0.21)	< 0.001	69 (0.14)	107 (0.22)	0.02
Liver cirrhosis	82,833 (13.3)	12,975 (25.9)	< 0.001	9645 (19.8)	12,724 (26.2)	0.15
Index year	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	, ( /	< 0.001		, ( - )	
2000	79,127 (12.7)	4233 (8.45)		4525 (9.30)	4151 (8.53)	0.03
2001	54,018 (8.67)	4360 (8.70)		3449 (7.09)	4282 (8.80)	0.06
2002	54,519 (8.75)	4512 (9.00)		3630 (7.46)	4413 (9.07)	0.06
2003	55,433 (8.90)	4164 (8.31)		3707 (7.62)	4056 (8.34)	0.03
2004	56,112 (9.01)	4570 (9.12)		4346 (8.93)	4441 (9.13)	0.007
2005	56,850 (9.13)	4589 (9.16)		4349 (8.94)	4453 (9.15)	0.007
2006	58,244 (9.35)	4619 (9.22)		4863 (10.0)	4491 (9.23)	0.007
2006	58,590 (9.41)				4491 (9.23) 4452 (9.15)	0.03
		4618 (9.21)		5084 (10.5)	, ,	
2008	59,650 (9.58)	4692 (9.36)		5352 (11.0)	4520 (9.29) 4652 (9.56)	0.06
2009	60,040 (9.64)	4837 (9.65)		5615 (11.5)	4652 (9.56)	0.06
2010	30,299 (4.86)	4928 (9.83)		3731 (7.67)	4740 (9.74)	0.07

Chi-square test.

and confounding remains likely, making clinical application hard to propose clearly. The authors spend more time justifying this study by discussing potential pathophysiologic overlap between these conditions. People who have sepsis may develop an acute inflammatory response and the concept of systemic inflammation might be associated with suicide attempts despite some investigators might criticize that no sound scientific rationale is provided. [16-18] It should be acknowledged that critically ill patients had more serious medical problems which might influence their suicide

COPD = chronic obstructive pulmonary disease, ESRD = end-stage renal disease.

<sup>\*</sup>A standardized mean difference (SMD) of ≤0.10 indicates a negligible difference between the 2 cohorts.

<sup>†</sup>Student's t-test.

<sup>‡</sup>New Taiwan Dollar (NTD), 1 NTD is equal to 0.03 USD.

<sup>§</sup>The urbanization level was divided by the population density of the residential area into 4 levels, level 1 was the most urbanized and level 4 was the least urbanized.

<sup>||</sup>Other occupation categories included those who were primarily retired, unemployed, and low-income populations.

Table 2
The incidences and risk factors for suicide with propensity score matching.

Variable	Event	PY	Rate*	Crude HR (95% CI)	Adjusted HR† (95% CI)
Critical illness					
No	11	269,117	0.41	1.00	1.00
Yes	29	183,740	1.58	3.81 (1.90–7.63)***	2.98 (1.46-6.08)**
Age group, years	10	00.550	1 44	0.00 (0.00 F.77)	
≤ 49 50–64	12 8	83,550 131,196	1.44 0.61	2.36 (0.96–5.77) 1.00	1.00
65+	20	238,111	0.84	1.36 (0.60–3.10)	1.00
Gender	20	200,111	0.01	1.00 (0.00 0.10)	
Women	21	191,925	1.09	1.51 (0.81-2.80)	
Men	19	260,932	0.73	1.00	1.00
Monthly income‡					
< 15,000	12	137,443	0.87	1.00	1.00
15,000 − 19,999 ≥ 20,000	25 3	212,671 102,743	1.18 0.29	1.35 (0.68–2.69) 0.34 (0.10–1.19)	
Urbanization level§	3	102,745	0.29	0.54 (0.10–1.19)	
1 (highest)	11	121,525	0.91	1.00	1.00
2	8	122,776	0.65	0.72 (0.29–1.79)	
3	10	77,610	1.29	1.42 (0.60–3.35)	
4 (lowest)	11	130,946	0.84	0.93 (0.40-2.14)	
Occupation category	45	470.040	0.05	4.00	1.00
Office worker	15 17	176,848	0.85	1.00	1.00
Laborer Other	17 8	190,042 85,967	0.89 0.93	1.06 (0.53–2.11) 1.10 (0.47–2.59)	
Comorbidity	O	05,307	0.95	1.10 (0.47 – 2.33)	
Schizophrenia					
No	39	450,014	0.87	1.00	1.00
Yes	1	2843	3.52	3.97 (0.55–28.9)	
Depression					
No	35	429,934	0.81	1.00	1.00
Yes Alcohol-related illness	5	22,923	2.18	2.67 (1.04–6.82)*	1.29 (0.45–3.71)
No	32	435,845	0.73	1.00	1.00
Yes	8	17,012	4.70	6.34 (2.91–13.8)***	3.86 (1.68–8.84)**
Anxiety		,		,	,
No	26	368,118	0.71	1.00	1.00
Yes	14	84,738	1.65	2.34 (1.22–4.50)*	1.56 (0.73–3.35)
Mental disorders	27	207 714	0.00	1.00	1.00
No Yes	37 3	397,714 55,143	0.93 0.54	0.58 (0.18–1.88)	1.00
Insomnia	3	55,145	0.54	0.30 (0.10 1.00)	
No	13	234,801	0.55	1.00	1.00
Yes	27	218,055	1.24	2.25 (1.16-4.38)*	1.42 (0.69-2.90)
Congestive heart failure					
No	37	426,810	0.87	1.00	1.00
Yes	3	26,047	1.15	1.29 (0.40–4.21)	
Hypertension No	17	206,556	0.82	1.00	1.00
Yes	23	246,301	0.93	1.13 (0.60–2.12)	1.00
Diabetes mellitus		,		(0.000 = 0.00)	
No	37	379,681	0.97	1.00	1.00
Yes	3	73,176	0.41	0.42 (0.13,1.35)	
Vascular diseases	07	040.000	0.05	1.00	1.00
No Yes	27 13	319,009 133,847	0.85 0.97	1.00	1.00
Non-ESRD CKD	13	133,047	0.97	1.14 (0.59–2.22)	
No	38	436.371	0.87	1.00	1.00
Yes	2	16,486	1.21	1.35 (0.33–5.62)	
ESRD				,	
No	40	449,715	0.89	1.00	1.00
Yes	0	3142	0.00	-	
COPD No	30	372,507	0.81	1.00	1.00
Yes	10	80,350	1.24	1.53 (0.75–3.15)	1.00
Malignancy	10	00,000	1.47	1.00 (0.10 0.10)	
No	39	437,350	0.89	1.00	1.00
Yes	1	15,507	0.64	0.68 (0.09-4.99)	
Autoimmune diseases		450.055	2.22	4.00	
No Yes	40	452,279	0.88	1.00	1.00
	0	578	0.00	-	

(Continued)

# Table2

## (Continued)

Variable	Event	PY	Rate*	Crude HR (95% CI)	Adjusted HR† (95% CI)
Liver cirrhosis					
No	24	356,119	0.67	1.00	1.00
Yes	16	96,738	1.65	2.45 (1.30-4.62)**	1.53 (0.77–3.02)

 $CI = confidence \ interval, COPD = chronic \ obstructive \ pulmonary \ disease, ESRD = end-stage \ renal \ disease, HR = hazard \ ratio; PY = person-years. The properties of the properties o$ 

## Table 3

Incidences and hazard ratios of suicide between individuals with and without critical illness stratified by demographics and comorbidity with propensity score matching.

			Criti	cal illness				
		No			Yes			
Outcome	Event	PY	Rate*	Event	PY	Rate*	Crude HR (95% CI)	Adjusted HR† (95% CI)
Age group, years								
≤64	3	122,652	0.24	17	92,094	1.85	7.35 (2.15, 25.1)**	5.52 (1.56, 19.5)**
65+	8	146,465	0.55	12	91,645	1.31	2.42 (0.99, 5.93)	1.95 (0.79, 4.83)
p for interaction								0.31
Gender								
Women	6	111,080	0.54	15	80,845	1.86	3.46 (1.34, 8.92)*	2.71 (1.03, 7.14)*
Men	5	15,837	0.32	14	102,895	1.36	4.13 (1.49, 11.5)**	3.17 (1.11, 9.08)*
p for interaction							, ,	0.76
Monthly income‡								
<15.000	5	82,892	0.60	7	54.551	1.28	2.14 (0.68, 6.78)	1.65 (0.51, 5.31)
15,000-19,999	4	120,538	0.33	21	92,133	2.28	6.68 (2.29, 19.5)***	5.37 (1.81, 16.0)**
≥20.000	2	65.687	0.30	1	37,056	0.27	0.91 (0.08, 10.1)	0.97 (0.09, 11.1)
p for interaction		,			,		,	0.74
Urbanization level§								
1 + 2 (higher)	7	148.847	0.47	12	95,454	1.26	2.68 (1.05, 6.83)*	1.98 (0.75, 5.18)
3 + 4 (lower)	4	120,270	0.33	17	88,286	1.93	5.61 (1.89, 16.7)**	4.57 (1.51, 13.9)**
p for interaction		,			,		,,	0.76
Occupation category								
Office worker	5	110.074	0.45	10	66.774	1.50	3.34 (1.14, 9.80)*	2.44 (0.80, 7.41)
Laborer	3	107.983	0.28	14	82,059	1.71	5.95 (1.71, 20.7)**	5.30 (1.50, 18.8)**
Other	3	51.060	0.59	5	34.907	1.43	2.37 (0.56, 9.93)	1.50 (0.34, 6.64)
p for interaction	Ü	01,000	0.00	Ü	0 1,001		2.0. (0.00, 0.00)	0.89
Comorbidity¶								0.00
No	2	77,287	0.26	1	11,976	0.83	3.55 (0.32, 39.2)	-
Yes	9	191.830	0.47	28	171.764	1.63	3.40 (1.60, 7.21)**	-
p for interaction	3	,	5.17	20	,,,,		0.10 (1.00, 1.21)	

CI = confidence interval; HR = hazard ratio; PY person-years.

attempts, or they might receive it due to injury from their suicide attempts. Both are important confounders that should be considered. Finally, it could also be argued that choosing the critical illness cohort as newly diagnosed may artificially select for those who seek more treatment with more medical visits, making more incidence of suicide attempts in the study group. However, the association remained after incorporating the competing risk methods; additionally, sepsis is

more susceptible to suicide attempts among these critically ill subjects, which might bring a new message and novel insights for the physicians caring for these specific groups. The appropriate position of this investigation in the literature might be reported with the above caveats as a justification for future research, and the detailed causal relationship and possible pathophysiological mechanism are strongly motivated.

<sup>\*</sup>Incidence rate per 10,000 person-years.

<sup>†</sup>Multivariable analysis included depression, alcohol-related illness, anxiety, insomnia, and liver cirrhosis.

<sup>‡</sup>New Taiwan Dollar (NTD), 1 NTD is equal to 0.03 USD.

<sup>\$</sup>The urbanization level was divided by the population density of the residential area into 4 levels, level 1 was the most urbanized and level 4 was the least urbanized.

<sup>||</sup>Other occupation categories included those who were primarily retired, unemployed, and low-income populations.

<sup>\*</sup>P < .05, \*\*P < .01, \*\*\*P < .001.

<sup>\*</sup> Incidence rate per 10,000 person-years.

<sup>†</sup>Multivariable analysis included depression, alcohol-related illness, anxiety, insomnia, and liver cirrhosis.

<sup>‡</sup>New Taiwan Dollar (NTD), 1 NTD is equal to 0.03 USD.

<sup>§</sup>The urbanization level was divided by the population density of the residential area into 4 levels, level 1 was the most urbanized and level 4 was the least urbanized.

 $<sup>\</sup>verb|||Other occupation categories included those who were primarily retired, unemployed, and low-income populations.$ 

<sup>¶</sup>Individuals with schizophrenia, depression, alcohol-related illness, anxiety, mental disorders, insomnia, congestive heart failure, hypertension, diabetes mellitus, vascular diseases, non-end-stage renal disease CKD, end-stage renal disease, chronic obstructive pulmonary disease, malignancy, autoimmune diseases, and liver cirrhosis were classified into the comorbidity group.

<sup>\*</sup>P < .05, \*\*P < .01,

<sup>\*\*\*</sup>P < .001.

Table 4

Comparisons of Incidence, and Hazard Ratios of suicide in different subtypes of critical illness compared to those without critical illness stratified by propensity score matching.

Variable	Event	PY	Rate*	Crude HR(95% CI)	Adjusted HR† (95% CI)
Without propensity score matching					
Critical illness					
None	291	4,026,154	0.72	1 (Reference)	1 (Reference)
Septicemia, septic shock	14	73,807	1.90	2.61 (1.53-4.47)***	2.53 (1.43-4.47)**
AMI	1	13,075	0.76	1.06 (0.15-7.53)	1.76 (0.24–13.0)
Hemorrhagic stroke	1	14,976	0.67	0.92 (0.13-6.57)	1.03 (0.14–7.40)
Ischemic stroke	13	84,175	0.76	2.13 (1.22–3.72)**	2.28 (1.25-4.17)**
With propensity score matching				,	
Critical illness					
None	11	269,117	0.41	1 (Reference)	1 (Reference)
Septicemia, septic shock	14	72.633	1.93	4.60 (2.09–10.2)***	3.43 (1.52–7.74)**
AMI	1	12,989	0.77	1.87 (0.24–14.5)	1.74 (0.22–13.5)
Hemorrhagic stroke	1	14.894	0.67	1.63 (0.21–12.6)	1.43 (0.18–11.1)
Ischemic stroke	13	83,224	1.56	3.80 (1.70–8.49)**	3.04 (1.34–6.90)**

CI = confidence interval, HR = hazard ratio, PY = person-years.

<sup>\*\*\*</sup>P < .001.

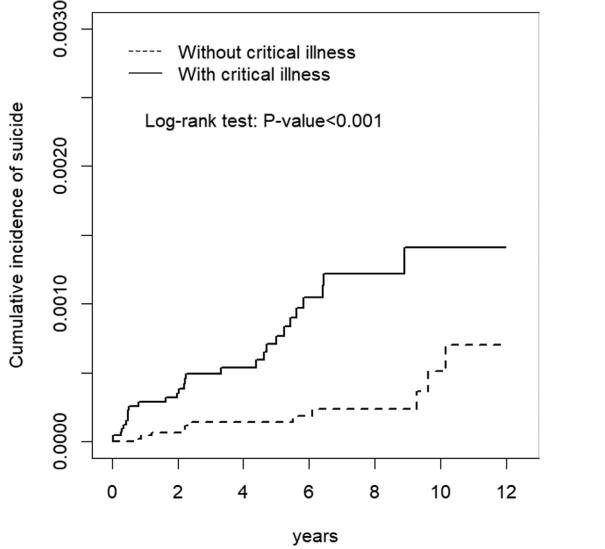


Figure 1. Cumulative incidence curves of suicide for groups with and without critical illness.

<sup>\*</sup>Incidence rate per 10,000 person-years.

 $<sup>{\ \ }^{\</sup>dagger} \text{Multivariable analysis included depression, alcohol-related illness, anxiety, insomnia, and liver cirrhosis.}$ 

<sup>\*\*</sup>P < .01,

## Table 5

Critical illness cohort to non-critical illness cohort subhazard ratio (SHR) of suicide estimated using the competing-risks regression models with propensity score matching.

# Competing risks regression models

	Critical illness		
	No	Yes	
Suicide			
Crude SHR (95% CI)	1 (Reference)	3.81 (1.92-7.55)***	
Adjusted SHR (95% CI)	1 (Reference)	2.98 (1.48-6.02)**	

Crude SHR, relative sub hazard ratio; adjusted SHR: multivariable analysis included depression, alcohol-related illness, anxiety, insomnia, and liver cirrhosis (death was also added in the model to measure adjusted SHR).

SHR = subhazard ratio.

#### 5. Limitations

Despite the idea and data being novel, certain limitations in this study should be addressed. First, the study probably cannot change practice since the limitations of the study and lack of applicability of its findings.

Second, it appears that the disease, comorbidity, and outcomes were identified by the ICD-9 code in the record. Some might worry this may not be overly specific despite this algorithm have been validated previously.

Indeed, the study is based on an insurance database. Therefore, an underestimation of the outcome is likely since those who died shortly or immediately after suicide may not be admitted to the hospital. Finally, the retrospective data-based secondary analysis has certain inherent limitations and the ideal study is prospective with the serial examination, but of course, is tricky to perform.

### 6. Conclusion

An association between critical illness and suicide attempts was shown. Sepsis/septic shock was found to confer the highest risk in these specific populations.

# **Author contributions**

Wei-Syun Hu - Study concept and design, acquisition of data, analysis and interpretation, drafting of the manuscript, critical revision of the manuscript for important intellectual content, and study supervision. Cheng-Li Lin- acquisition of data, analysis, and interpretation.

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<sup>\*\*</sup>P < .01,

<sup>\*\*\*</sup>P < .001.