# The association between depression and length of stay in the intensive care unit

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**Abstract**

Depression is common after patients are discharged from the intensive care unit (ICU) and has a negative impact on quality of life and mortality. There is inconsistent information about ICU admission and the risk of depression. The aim of our study was to investigate the association between the risk of depression and length of ICU stay.

ICU survivors between 20 and 65 years old were enrolled in this study using data from Taiwan's nationwide population database. All study subjects were followed for a maximum of 1 year or until they were diagnosed with new-onset depression. The association between the length of ICU stay and the depression risk among ICU survivors was estimated using a Cox regression model. The screened diagnostic records of ICU survivors with depression were also investigated to find the potential disease effect of depression.

Compared to patients with ICU stays between 8 and 14 days, the adjusted HR (95% confidence interval) for depression in patients with ICU stays between 1 to 3 days, 4 to 7 days, 15 to 21 days, and ≥22 days were 1.08 (1.03–1.13), 1.01 (0.96–1.05), 1.08 (1.01–1.14), and 1.12 (1.06–1.19), respectively. For patients with depression after discharge from the ICU, the most common primary diagnosis was intracerebral hemorrhage.

There is a risk of depression after ICU discharge, and the incidence of depression may be higher among patients between 20 and 49 years old. The risk of depression was U-shaped, with higher risks associated with ICU stays of 1 to 3 days and more than 15 days.

**Abbreviations:** ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification, ICU = intensive care unit, NHIRD = National Health Insurance Research Database.

**Keywords:** depression, intensive care unit, National Health Insurance Research Database

## 1. Introduction

Depression is one of the important causes of illness and disability in adolescents and adults. In the past few years, an increasing number of survivors have been discharged from intensive care units (ICUs). Patients recovering from critical illness, physical dysfunction, and organ failure may experience psychological and cognitive dysfunction after discharge, which is called post-intensive care syndrome.[1] A previous study showed that depressive symptoms are common in patients discharged from the ICU and have a negative impact on quality of life.[2] Systematic reviews showed that approximately 30% of ICU survivors had clinically important depressive symptoms in the first 12 months after severe disease.[2]

Symptoms of depression hinder patients from performing physical work and act as a barrier to social participation.[2] In addition, the overall 5-year mortality rate was 3.4 times higher among patients discharged from the ICU compared with the general population,[3] and there are correlations between depression and the risks of mortality and morbidity, both in the general population and among patients with comorbidities.[4]

The risk factors for depression in the first year after acute respiratory distress syndrome include female sex, younger age, unemployment, alcoholism, and greater opioid use in the ICU, while a greater severity of disease and longer ICU stays were not correlated with depression.[5] Parker et al showed that the risk factors for posttraumatic stress disorder included psychopathological history, the use of benzodiazepines, and early memories of frightening ICU experiences.[6]

In addition to these risk factors, we hypothesized that the duration of ICU stay may play an important role in psychological problems. The aim of our study was to clarify the relationship between the length of ICU stay and the occurrence of depression.

## 2. Methods

### 2.1. Data source

The Taiwan's National Health Insurance Research Database (NHIRD) was used in a retrospective nationwide population-based cohort study. The NHIRD was established for research purposes and includes detailed healthcare services information, including all payments for outpatient visits, hospitalizations, and prescriptions for each patient who participates in the national health insurance program that provides coverage for over 99% of the residents of Taiwan.[7] This claim database uses the Internal Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) to archive each patient's outpatient visits or hospitalization diagnostic records, which can be linked to the prescriptions and procedures. Each individual's unique personal identification number in the NHIRD is interlinked with all the datasets, and all data used in this study were deidentified. The study was approved by the institutional review board (IRB) of the Chi Mei Medical Center (IRB no: 10411-E01).

### 2.2. Study population

ICU survivors were identified as the study subjects. ICU patients were recognized by to the medical expenditure applications, and those patients who stayed in the ICU between 2000 and 2013 were enrolled in this study. The study subjects were defined as those with a survival duration after discharge from the ICU of more than 1 year and an age between 20 and 65 years. The exclusion criteria were

(1) patients with a disease history of psychotic episodes/ depression/anxiety before and during the ICU stay;
(2) patients with mortality records during the follow-up period;
(3) patients with a record of hospitalization for longer than 1 year;
(4) patients with records of machine ventilation and ECMO;
(5) ICU survivors with anxiety/depression records after the follow-up; and
(6) the groups of patients with dementia and cancer, as they have a potentially high risk of depression.

Figure 1 shows the flowchart of subject selection.

The baseline covariates included age, sex, Charlson comorbidity index (CCI) score, trauma (ICD-9-CM code: 800-949), and metabolic syndrome diseases, including hypertension (HTN) (ICD-9-CM code 401–405), diabetes mellitus (DM) (ICD-9-CM code 250), and hyperlipidemia (ICD-9-CM code 272). Age was grouped into 3 categories: 20 to 34, 35 to 49, and 50 to 65 years. The CCI was used to summarize important concomitant diseases based on the ICD-9-CM codes.[8] The diseases included in the CCI, trauma, and metabolic syndrome diseases were defined by 3 related outpatient visits or 1 inpatient admission within 1 year prior to the first ICU admission date.

### 2.3. Measurements

The outcomes of interest in this study were patients with a new-onset diagnosis of depression (ICD-9-CM code: 300.4, 309.2, 309.3, 309.4, 296.2, 296.5, 300.4, 309.0, 309.1, 296.82, 300, and 311). The depression diagnosis was defined by 3 related outpatient visits or 1 inpatient admission after the ICU admission date. All selected ICU survivors were right censored on December 31, 2013, or on the date they received the diagnosis of depression. The patients were followed for a maximum of 1 year.

According to the study aims, the length of ICU stay and length of hospital stay for ICU survivors with new-onset depression were major concerns in this study. The length of ICU stay was categorized as 1 to 3 days, 4 to 7 days, 8 to 14 days, 15 to 21 days, and ≥22 days.[9] The length of hospital stay was categorized as fewer than 14 days and more than 14 days.[10] The medical records of ICU survivors with depression were screened to identify the potential factors affecting the incidence of depression.

### 2.4. Statistical analysis

The categorical variables are presented as frequencies with percentages, and the continuous variable, age, is shown as the mean with standard deviation. Pearson Chi-squared test and Student $t$ test were used to compare the differences between patients with depression and those without depression. The risk of depression among patients with different ICU stay durations was estimated using Cox regression analysis with adjusted variables, including age, sex, and comorbidities. The trends of the cumulative risk of the incidence of depression after ICU discharge among patients with different durations of ICU stays were plotted, and the log-rank test was used to compare the differences. SAS statistical software (version 9.4; SAS Institute, Inc., Cary, NC) was used to perform all statistical analyses. Kaplan-Meier curves were generated using STATA (version 12; Stata Corp. College Station, TX). All significance levels were set at $P < .05$.

## 3. Results

A total of 15,545 patients with depression were enrolled. The mean age of the patients was 46.49 years, and 58.2% were male. Metabolic syndrome patients accounted for 41.66%, and 45.4% of patients had a history of trauma. We further divided our study period into 3 periods: before 2005, 2005 to 2009, and after 2009. This variable was also used to adjust the risk of depression in the model. The median time from ICU discharge to depression was 3.13 months (Table 1).

The length of ICU stay (percentage of patients with depression) were as follows: 1 to 3 days (28.15%), 4 to 7 days (24.02%), 8 to
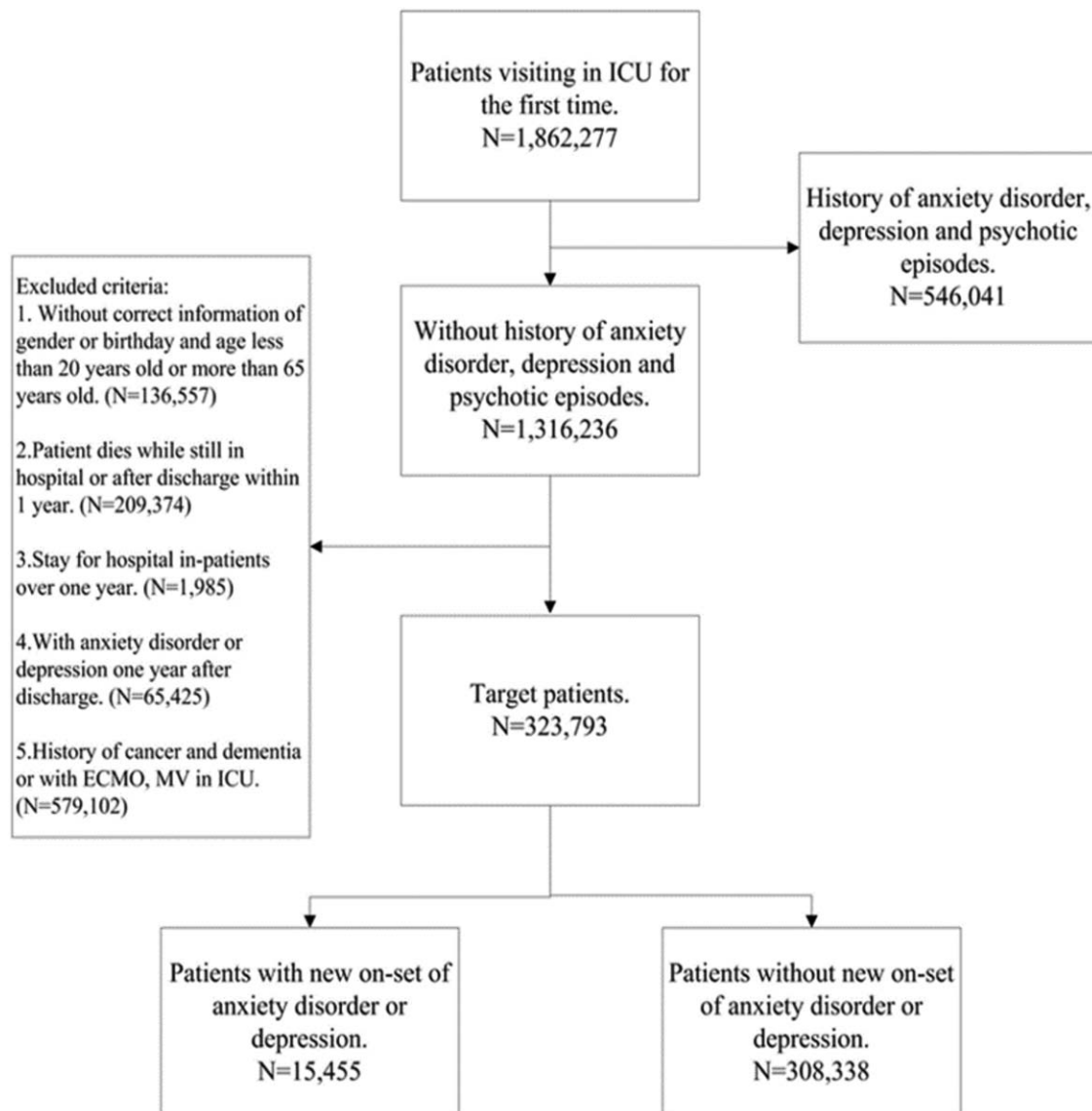
**Figure 1.** Flow chart of patients included in the study.

14 days (22.09%), 15 to 21 days (11.66%), and ≥22 days (14.08%). Most patients with depression had a hospital stay that lasted fewer than 14 days (55.57%) (Table 2).

Compared to patients with ICU stays between 8 and 14 days, the adjusted HRs (95% confidence interval) for depression in patients with ICU stays that were 1 to 3 days, 4 to 7 days, 15 to 21 days, and ≥22 days were 1.08 (1.03–1.13), 1.01 (0.96–1.05), 1.08 (1.01–1.14), and 1.12 (1.06–1.19), respectively. Considering of the possible bias, we added the diagnosis of depression defined by psychiatrists. This sensitivity analysis presented the similar results. ICUs of the study include internal ICU, surgical ICU, neurological ICU, neurosurgical ICU, and others. We had added the analysis among different ICUs, accordingly (Table 3).

In the separate analysis of patients 20 to 34 years old, compared to patients with ICU stays of 8 to 14 days, the adjusted HRs (95% confidence interval) for depression in patients with ICU stays of 1 to 3 days, 4 to 7 days, 15 to 21 days, and ≥22 days were 1.16 (1.05–1.29), 0.91 (0.82–1.01), 1.17 (1.01–1.34), and

1.31 (1.14–1.49). For male patients, the risk of depression was higher in those with ICU stays of 15 to 21 days and ≥22 days than in those with ICU stays of 8 to 14 days, with the adjusted HRs (95% confidence interval) of 1.11 (1.03–1.21) and 1.27 (1.18–1.37). Figure 2 shows the cumulative incidence rate of depression among patients with different durations of ICU stays.

Table 4 shows that the most common primary diagnoses in all ICU patients were subarachnoid, subdural, and extradural hemorrhage following injury; intracerebral hemorrhage; chronic ischemic heart disease; septicemia; and occlusion of the cerebral arteries. For patients with depression after discharge from the ICU, the most common primary diagnoses were intracerebral hemorrhage; subarachnoid, subdural, and extradural hemorrhage following injury; chronic ischemic heart disease; occlusion of cerebral arteries; and fracture of the base of the skull. Table 5 shows the primary diagnoses among patients with different ICU stay durations. Figure 3 showed the association between incidence rate of depression and length of stay in ICU.

## Table 1

**Patients characteristic after the first intensive care unit hospitalization with and without depression.**

| | With depression N = 15,455 | Without depression N = 308,338 | P-value |
|---|---|---|---|
| Age, yr (mean ± SD) | 46.49 ± 12.35 | 43.21 ± 13.15 | <.0001 |
| Age groups | | | <.0001 |
| 20–34 | 3198 (20.69) | 99,633 (32.31) | |
| 35–49 | 4984 (32.25) | 91,576 (29.70) | |
| 50–65 | 7273 (47.06) | 117,129 (37.99) | |
| Gender (%) | | | .0018 |
| Male | 8995 (58.20) | 183,353 (59.46) | |
| Female | 6460 (41.80) | 124,985 (40.54) | |
| Comorbidities | | | |
| Metabolic syndrome | 6439 (41.66) | 9016 (58.34) | <.0001 |
| Hypertension | 5062 (32.75) | 76,554 (24.83) | |
| Diabetes | 2586 (16.73) | 51,688 (16.76) | |
| Hyperlipidemia | 1974 (12.77) | 32,881 (10.66) | |
| Trauma | 7017 (45.40) | 114,274 (37.06) | <.0001 |
| CCI scores | | | <.0001 |
| 0 | 7839 (50.72) | 182,413 (59.16) | |
| 1≥ | 7616 (49.28) | 125,925 (40.84) | |
| Department of medical | | | |
| Internal | 4496 (29.09) | 82,772 (26.84) | <.0001 |
| Surgical | 2291 (14.82) | 54,456 (17.66) | |
| Neurology | 1049 (6.79) | 10,967 (3.56) | |
| Neurosurgery | 4965 (32.13) | 73,674 (23.89) | |
| Others | 2654 (17.17) | 86,469 (28.04) | |
| Diagnosed year period | | | |
| Before 2005 | 2932 (18.97) | 41,106 (13.33) | <.0001 |
| 2005 to 2009 | 7440 (48.14) | 140,856 (45.68) | |
| After 2009 | 5083 (32.89) | 126,376 (40.99) | |
| Diagnosed depression in psychiatry | 6371 (41.22) | | |
| Time to depression, mo | | | |
| Median (Q1–Q3) | 3.13 (0.90–6.60) | | |

## Table 2

**Medical utilization during the first ICU hospitalization with and without depression.**

| | With depression N = 15455 | Without depression N = 308338 | P-value |
|---|---|---|---|
| Length of ICU stay | | | <.0001 |
| 1–3 d | 4350 (28.15) | 91,900 (29.80) | |
| 4–7 d | 3713 (24.02) | 81,882 (26.56) | |
| 8–14 d | 3414 (22.09) | 71,377 (23.15) | |
| 15–21 d | 1802 (11.66) | 29,348 (9.52) | |
| ≥22 d | 2176 (14.08) | 33,831 (10.97) | |
| Length of hospital stay | | | <.0001 |
| <14 d | 8588 (55.57) | 195,556 (63.42) | |
| ≥14 d | 6867 (44.43) | 112,782 (36.58) | |

## 4. Discussion

To the best of our knowledge, this is the first study to use a national claims database to investigate the association between length of stay in the ICU and depression. We found a U-shaped association between the length of stay in the ICU and the risk of depression. The risk of depression was the highest in patients with ICU stay durations longer than 21 days followed by those with stays of 15 to 21 days and then 1 to 3 days when compared with patients with ICU stay durations of 8 to 14 days. This U-shaped association was also observed in patients 20 to 34 and 35 to 49 years old but not in those 50 to 65 years old. In male patients, the longer the length of stay in the ICU, the higher the risk of depression was. In females, the length of ICU stay did not have an impact on the risk of depression.

ICUs are psychologically challenging environments; patients in the ICU may be frightened by high-pitched alarms that beep sporadically; if patients have endotracheal tubes, then they cannot communicate with people, and many patients have intravascular lines in their arm or leg, Foley catheters in their

## Table 3

**Risk factor for depression after first time ICU hospitalization.**

| | Length of ICU stay | | | | |
|---|---|---|---|---|---|
| | 1–3 d | 4–7 d | 8–14 d | 15–21 d | ≥22 d |
| Stratification | | | Adjusted HR (95% C.I.) | | |
| Overall | 1.08* (1.03–1.13) | 1.01 (0.96–1.05) | Ref. | 1.08* (1.01–1.14) | 1.12* (1.06–1.19) |
| Diagnosed depression in psychiatry | 1.10* (1.03–1.19) | 0.96 (0.89–1.04) | Ref. | 1.11* (1.01–1.23) | 1.12* (1.02–1.23) |
| Age groups | | | | | |
| 20–34 | 1.16* (1.05–1.29) | 0.91 (0.82–1.01) | Ref. | 1.17* (1.01–1.34) | 1.31** (1.14–1.49) |
| 35–49 | 1.11* (1.03–1.21) | 1.04 (0.95–1.13) | Ref. | 1.12* (1.00–1.25) | 1.23** (1.11–1.37) |
| 50–65 | 0.97 (0.91–1.05) | 1.01 (0.94–1.08) | Ref. | 1.03 (0.94–1.13) | 1.02 (0.94–1.12) |
| Gender | | | | | |
| Male | 0.97 (0.91–1.03) | 0.99 (0.92–1.05) | Ref. | 1.11* (1.03–1.21) | 1.27** (1.18–1.37) |
| Female | 1.19** (1.11–1.27) | 1.01 (0.94–1.09) | Ref. | 1.05 (0.95–1.15) | 0.97 (0.89–1.07) |
| ICU Unit | | | | | |
| Internal | 1.16* (1.06–1.27) | 1.10 (1.00–1.21) | Ref. | 1.09 (0.93–1.27) | 0.99 (0.86–1.15) |
| Surgical | 0.88* (0.78–0.99) | 0.94 (0.83–1.06) | Ref. | 1.12 (0.96–1.31) | 1.38** (1.19–1.61) |
| Neurological | 0.98 (0.81–1.18) | 0.89 (0.74–1.07) | Ref. | 1.14 (0.92–1.42) | 1.00 (0.81–1.25) |
| Neurosurgical | 0.79** (0.73–0.87) | 0.89* (0.82–0.96) | Ref. | 1.01 (0.91–1.12) | 1.02 (0.92–1.12) |
| Others | 1.11 (0.99–1.26) | 1.04 (0.93–1.16) | Ref. | 1.01 (0.89–1.15) | 1.24* (1.10–1.40) |

[a] Baseline variables were included in adjusted covariates.

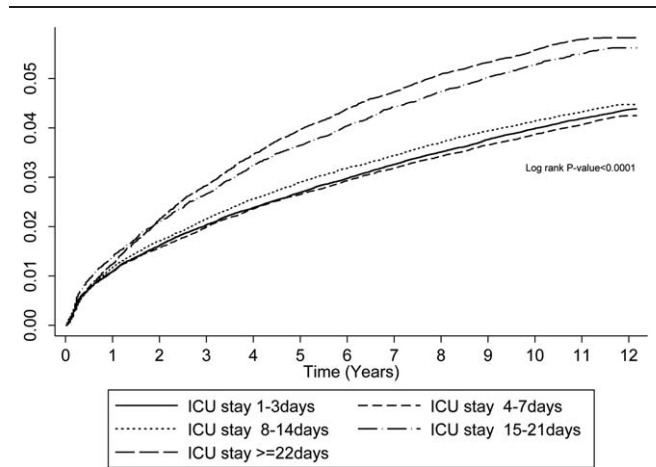* as P-value < .05.

** as P-value < .0001.

**Figure 2.** Cumulative incidence rate of depression among patients with different intensive care unit stay durations.

**Table 4**

**Primary diagnosed in patients with depression.**

| Primary diagnosed in ICU | | | | |
|---|---|---|---|---|
| **Overall** | **N (%)** | **Depression patients** | **N (%)** |
| Subarachnoid, subdural, and extradural hemorrhage, following injury | 23156 (7.15) | Intracerebral hemorrhage | 1725 (11.16) |
| Intracerebral hemorrhage | 21277 (6.57) | Subarachnoid, subdural, and extradural hemorrhage, following injury | 1482 (9.59) |
| Other forms of chronic ischemic heart disease | 14817 (4.58) | Other forms of chronic ischemic heart disease | 754 (4.88) |
| Septicemia | 8253 (2.55) | Occlusion of cerebral arteries | 736 (4.76) |
| Occlusion of cerebral arteries | 7940 (2.45) | Fracture of base of skull | 436 (2.82) |

urethra and physical restraints. These experiences make patients suffer a loss of dignity; they may feel helpless, sad, powerless, punished, embarrassed, and violated, and these feelings could trigger depression after their discharge from the ICU.

Wang et al[11] reported that patients with depressive symptoms after ICU discharge were younger, less likely to have cardiac disease, more likely to have had a previous history of depression and more likely to use an antidepressant on hospital admission and discharge. A large retrospective analysis of Danish ICU survivors also found that patients with pre-ICU compromised physical functioning and depression had more severe depression postdischarge and that those with a previous depression history were more likely to have premorbid psychiatric diagnoses compared with the general population.[12]

Our study surveyed new depression cases among ICU survivors for 1 year after discharge and excluded patients with a depression history or depression diagnosed during hospitalization.

Wang et al[11] found that younger patients had a higher risk of depressive symptoms independent of antidepressant use status. Studies about the correlation between age and depression in ICU survivors have varied in their conclusions. Weinert et al found

that older age was associated with more depressive symptoms after discharge for 1 year and that depressive symptoms were prevalent among both younger and older patients.[2]

Other systematic reviews did not show a correlation between post-ICU depression and age.[13,14] These differences may be due in part to variations in inclusion criteria. Our study focused on the length of ICU stay and depression after a first ICU admission. We found that patients aged 20 to 49 years had an association between depression and ICU stay duration. The association was U-shaped, and a lower risk of depression was observed in the patients with lengths of ICU stay between 4 and 14 days. For patients aged 50 to 65 years, there was no correlation between depression and the length of ICU stay.

In our study, we found that the most important diagnoses related to depression after ICU discharge were intracerebral, subarachnoid, subdural, and extradural hemorrhage. Brain damage has a substantial impact on depression after patient discharge. This is consistent with the findings of previous studies. Brain injury may result in long-term disability of physical, cognitive, and psychosocial functioning.[15] Patients also experience difficulty remaining employed in the same occupation,

**Table 5**

**Primary diagnosed in different length of ICU stay.**

| Length of ICU stay | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 1–3 d | N (%) | 4–7 d | N (%) | 8–14 d | N (%) | 15–21 d | N (%) | ≥22 days | N (%) |
| Other forms of chronic ischemic heart disease | 9690 (2.99) | Subarachnoid, subdural, and extradural hemorrhage, following injury | 7124 (2.20) | Intracerebral hemorrhage | 5516 (1.70) | Intracerebral hemorrhage | 2933 (0.91) | Intracerebral hemorrhage | 4110 (1.27) |
| Subarachnoid, subdural, and extradural hemorrhage, following injury | 6479 (2.00) | Intracerebral hemorrhage | 5116 (1.58) | Subarachnoid, subdural, and extradural hemorrhage, following injury | 4908 (1.52) | Subarachnoid, subdural, and extradural hemorrhage, following injury | 2024 (0.63) | Subarachnoid, subdural, and extradural hemorrhage, following injury | 2621 (0.81) |
| Intracerebral hemorrhage | 3602 (1.06) | Other forms of chronic ischemic heart disease | 2528 (0.78) | Septicemia | 2340 (0.72) | Occlusion of cerebral arteries | 1297 (0.40) | Other diseases of lung | 1881 (0.58) |
| Cardiac dysrhythmias | 2692 (0.83) | Diabetes mellitus | 2359 (0.73) | Occlusion of cerebral arteries | 2163 (0.67) | Septicemia | 986 (0.30) | Occlusion of cerebral arteries | 1325 (0.41) |
| Intervertebral disc disorders | 2237 (0.69) | Septicemia | 2061 (0.64) | Fracture of base of skull | 1979 (0.61) | Fracture of base of skull | 945 (0.29) | Fracture of base of skull | 1254 (0.39) |
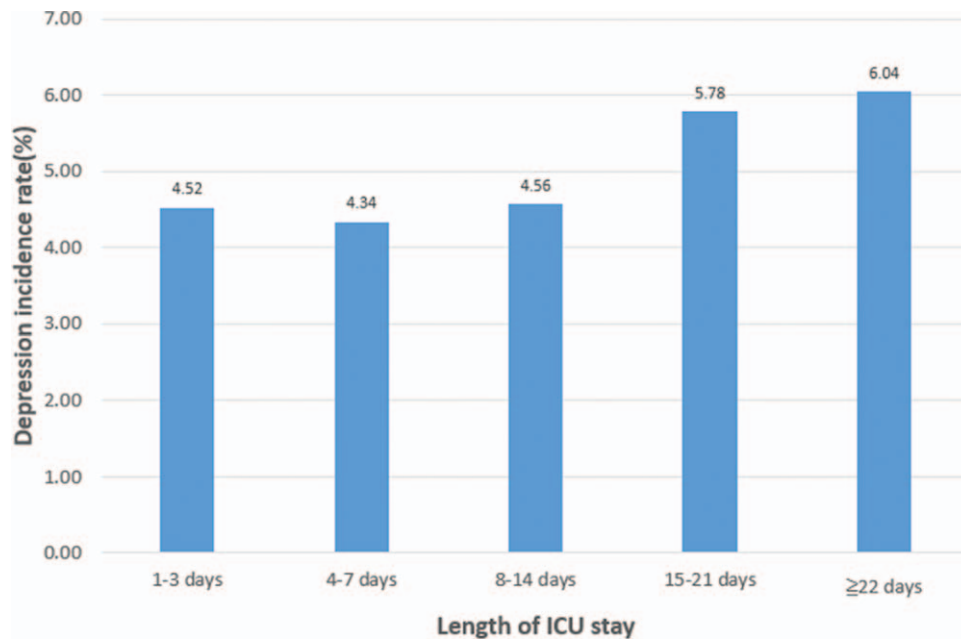
**Figure 3.** The association between incidence rate of depression and length of stay in intensive care unit.

having and maintaining social relationships, and fulfilling their true social function.[16] In addition to cognitive sequelae and psychiatric problems, anxiety disorders combined with alcohol use disorders may contribute to depression.[17]

It is important to detect and recognize depression because it may lead to poor quality of life following ICU discharge; furthermore, depression is potentially treatable and preventable. Depression is related to a poor quality of life after a critical illness, and a previous study also showed that depression increases mortality.[17]

From our study, we found that the common diagnoses among patients with depression were cerebrovascular disease, included intracerebral hemorrhage, subarachnoid, subdural, and extra-dural hemorrhage, occlusion of cerebral arteries, and chronic ischemic heart disease. Depression starts after a major life change or trauma. We suggest physicians to pay attention to this population and psychotherapy may help individuals recover from depression. Cognitive behavioral therapy and interpersonal therapy can help patients learn ways to better cope with stress and manage their symptoms of depression. These strategies can lead to recovery and enable patients to function at their best. Males having greater depression rates and in the age group of 20 to 49 is more significant and relatable as younger males may have the burden of supporting their family, which if they were unable to do so due to the aftermath of the disease process may have resulted in depression. So again, socio-economic factors and disease process probably are more significant than the length of ICU stay. Patients above 50 years had lower rates, that too may go along with the fact that by that age their socio-economic responsibilities were less.

### 4.1. Limitations

Our study has several limitations. First, our database does not include information on disease severity in patients admitted to the ICU. Our study could not examine whether greater disease

severity in the ICU was associated with a higher risk of depression because ICU severity data were not available. Second, information on some risk factors for depression was not available in the claims data, such as education level, true income, alcohol use, smoking, physical activity, and emotional abuse. These factors may have confounded the observed association between depression and ICU stay. Third, our diagnosis of depression was based on physician coding of the diagnosis using ICD-9 codes. The clinical criteria for depression listed in the Diagnostic and Statistical Manual of Mental Disorders, including current patient symptoms and patient history, were not obtained. It may be a limitation about underestimation of patients with depression in this study. Patients who did not seek treatment for depression will not be recorded in this claims database. Patients with depression in this study were identify as health care seeking behavior for depression treatment.

### 5. Conclusions

Our study suggests that there is risk of depression following the care of a critical illness in the ICU and that depression may be more common among patients 20 to 49 years old. The association between depression and length of ICU stay was U-shaped, with a greater risk of depression in patients with ICU stays of 1 to 3 days and more than 15 days. Physicians need to recognize and monitor symptoms of depression after ICU stays.

### Author contributions

All authors have read and approved the final manuscript.
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**Writing – review & editing:** Kuang-Ming Liao, Chin-Ming Chen, Kuo-Chen Cheng.

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